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No. 90-1898

In the Supreme Court of the United States

OCTOBER TERM, 1991

ABBOTT LABORATORIES, PETITIONER

v.

DAVID A. KESSLER, M.D., COMMISSIONER

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE DISTRICT OF COLUMBIA CIRCUIT

BRIEF FOR THE RESPONDENT IN OPPOSITION

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QUESTION PRESENTED

Whether the court of appeals properly determined that provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 defining the eligibility of certain drugs for periods of limited protection from streamlined approval of generic copies (21 U.S.C. 355(j)(4)(D)(i) and (v)) are ambiguous, and that this matter therefore should be remanded to the Food and Drug Administration to choose among reasonable constructions of the statutory language.

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-24a) is reported at 920 F.2d 984. The memorandum and order of the district court (Pet. App. 38a-61a) are reported at 691 F. Supp. 462. The district court's memorandum and order disposing of post-judgment motions (Pet. App. 25a-37a) are unreported.

JURISDICTION

The judgment of the court of appeals was entered on December 7, 1990. A petition for rehearing was denied on March 14, 1991. Pet. App. 100a-101a. The petition for a writ of certiorari was filed on June 12, 1991. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

1. The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, often referred to as the Hatch-Waxman Amendments, made several major changes in the law concerning approval and marketing of new drugs. Title I established streamlined procedures—dispensing with the expensive and time-consuming clinical trials usually required—for approval by FDA of generic copies of previously approved drugs and for approval of new drugs based on published research data. 21 U.S.C. 355(j) and 355(b)(2). Under these procedures, a manufacturer may obtain approval to market a drug without performing the clinical tests normally required to support a full new drug application ("NDA") either by relying on clinical trials for a previously approved drug (the abbreviated new drug application or "ANDA" procedure) or by relying on published data in the scientific literature (the so-called "paper" NDA procedure). Title I also provides varying periods of marketing "exclusivity" for innovative drugs approved on the basis of new clinical testing. During these periods, FDA approvals of any abbreviated applications or "paper" NDAs will not be effective. 21 U.S.C. 355(j)(4)(D) and 355(c)(3)(D).[1] Title II of the Hatch-Waxman Amendments provides for extension of the patent term of drugs meeting certain conditions to compensate for the period of patent life lost during FDA's pre-approval review process. 35 U.S.C. 156.

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[1] The relevant statutory language defining the period of market exclusivity for a particular product is the same for both ANDAs and "paper" NDAs. For clarity, we will refer only to the ANDA provisions in the remainder of this brief.

2. This case arises out of the denial by FDA of a citizen petition submitted by petitioner seeking ten years of market exclusivity under Title I of the Hatch-Waxman Amendments for Depakote, one of its drug products. Pet. App. 5a, 62a-99a. Under Title I, five categories of drugs are eligible for periods of market exclusivity ranging from two to ten years. 21 U.S.C. 355(j)(4)(D)(i)-(v). The period of market exclusivity applicable to Depakote is determined under one of two categories applicable to drugs approved during a "window period" prior to enactment of the Hatch-Waxman Amendments.[2] Petitioner contends that Depakote is entitled to the maximum ten-year period of exclusivity, under 21 U.S.C. 355(j)(4)(D)(i). The FDA found that the product is instead entitled only to two years of exclusivity—a period that has already expired. 21 U.S.C. 355(j)(4)(D)(v).

The ten-year provision applies to drugs approved during the "window period" that contain "no active ingredient (including any ester or salt of the active ingredient)" that has previously received FDA approval. 21 U.S.C. 355(j)(4)(D)(i).[3] In contrast, the two-year provision applies to drugs approved during the "window period" that do contain "an active ingredient (including any ester or salt of the active

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[2] The "window period" extended from January 1, 1982 through September 24, 1984 (the date the statute was enacted).

[3] Such drugs approved after the "window period" are entitled to five years' exclusivity. 21 U.S.C. 355(j)(4)(D)(ii).

Esters and salts are chemical compounds formed by reactions between a "parent" substance and another chemical. An ester is formed by the reaction of an acid with an alcohol. A salt is formed when the hydrogen of an acid is replaced by a metal or its equivalent. Pet. App. 5a.

ingredient)" that has been previously approved by FDA. 21 U.S.C. 355(j)(4)(D)(v).[4]

3. In 1978 FDA approved petitioner's new drug application for Depakene, an anticonvulsant drug for control of seizures in epileptics and others. Pet. App. 4a. Valproic acid is Depakene's "active ingredient" —the form of the therapeutic agent in the drug prior to administration to a patient. That acid is also its "active moiety"—the pharmaceutically active chemical which produces the therapeutic effect in the body after administration to the patient. *Ibid.* In 1982 FDA approved petitioner's new drug application for Depakote, another anticonvulsant drug. Depakote's active ingredient is divalproex sodium. Depakote breaks down in the body to valproic acid, and that substance achieves the drug's therapeutic effect. *Ibid.* Thus, Depakote has the same active moiety (valproic acid) as petitioner's earlier product, Depakene. Accordingly, petitioner sought and obtained FDA approval of Depakote by relying on the clinical studies of safety and efficacy that it had submitted for Depakene. *Ibid.*

Following passage of the Hatch-Waxman Amendments, FDA determined that petitioner was entitled to two years of marketing exclusivity for Depakote. Petitioner challenged that determination administratively by filing a citizen petition with the agency, seeking a ruling that Depakote was instead entitled to ten years of exclusivity. Pet. App. 5a.

FDA denied the petition, concluding first that divalproex sodium (the active ingredient of Depa-

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[4] Such drugs approved after the "window period" are entitled to no exclusivity at all, unless their approval is based on some new clinical investigations. In that latter event, the drugs are entitled to three years' exclusivity. 21 U.S.C. 355(j)(4)(D)(iii) and (iv).

kote) is a salt of valproic acid (the active ingredient of petitioner's own previously approved product, Depakene) and not, as petitioner contended, a totally new chemical substance. Pet. App. 5a, 67a-77a. FDA then rejected petitioner's argument that even if divalproex sodium is a salt of valproic acid, Depakote nevertheless qualified for ten years' exclusivity because neither divalproex sodium nor any ester or salt *of it* had been previously approved. The agency explained that it interpreted the entire phrase "active ingredient (including any ester or salt of the active ingredient)" in the exclusivity provisions of the Hatch-Waxman Amendments to refer to the "active moiety" of the drug. *Id.* at 85a. The agency specifically interpreted Congress's use of the word "including" to indicate that the parenthetical portion of the phrase was not an exhaustive list of the additional substances that were comprehended by the phrase as a whole but rather a list of "examples of the types of minor variations in chemical structure that Congress did not intend to reward with exclusivity." *Ibid.* Accordingly, because Depakote and the previously approved drug Depakene shared the same active moiety, FDA determined that Depakote was not entitled to ten years' market exclusivity.

4. Petitioner challenged FDA's denial of its citizen petition by filing this action in the district court. The district court observed that if it concluded—as it believed FDA had—that the term "active ingredient" in the ten-year exclusivity provision referred to the drug's active moiety, then Depakote plainly would not qualify for the maximum ten-year period of market protection (because its active moiety, valproic acid, had been previously approved). Pet. App.

55a-56a.[5] The court also noted that if, as petitioner urged, "active ingredient" referred instead to an ingredient in the final dosage form of the drug, Depakote would meet the requirements for ten years' exclusivity (because neither divalproex sodium nor any ester or salt *of it* had been previously approved). *Id.* at 56a.

The district court found it unnecessary to choose between these two interpretations, however, because it concluded that even if petitioner's final dosage form approach were correct, Depakote would fall within the literal terms of *both* the ten-year and the two-year exclusivity provisions (a position advocated by neither party). Pet. App. 56a. This apparent conflict could be resolved, in the district court's view, by resort to the legislative purpose of the Hatch-Waxman Amendments, *i.e.*, to reward substantial investment in new drug development. Because petitioner had not undertaken new clinical investigations to support its application for Depakote, but rather had relied on investigations performed in development of another previously approved drug, the district court concluded that petitioner's investment in Depakote did not warrant the lengthier ten-year period of exclusivity. *Id.* at 57a-59a. Thus, the district court held that regardless of which interpreta-

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[5] FDA never contended that the bare term "active ingredient" meant "active moiety." Rather, the agency interpreted the term "active ingredient" as modified by the parenthetical reference to salts and esters—the way it appears in the exclusivity provisions—to mean "active moiety." FDA noted that this interpretation was consistent with earlier agency decisions more narrowly construing "active ingredient" elsewhere in the Hatch-Waxman Amendments, where the term appears unmodified by any reference to related chemical entities. Pet. App. 82a-83a.

tion of the term "active ingredient" it applied, Depakote was entitled only to two years of exclusive marketing.

5. The court of appeals rejected the statutory interpretations of both parties and remanded the matter to the agency for a new construction of what the court concluded was ambiguous language in the statute. Focusing on the phrase "active ingredient (including any ester or salt of the active ingredient)" in 21 U.S.C. 355(j)(4)(D)(v), the court pointed out that it is not clear whether the "active ingredient" referred to in the parenthetical portion of that phrase refers to the active ingredient of the drug under consideration for a period of exclusivity or the active ingredient of a previously approved drug. Pet. App. 7a. Noting that the statutory scheme requires that a given drug's eligibility for a period of exclusivity be determined by comparing it to *all* previously approved drugs, the court of appeals explained that Congress may have intended the parenthetical portion of the phrase to refer to esters and salts of *any* previously approved active ingredient. *Id.* at 8a.

Observing that nothing in the legislative history reveals Congress's intent concerning the meaning of this ambiguous language (Pet. App. 8a), the court of appeals nevertheless rejected FDA's conclusion that the entire phrase "active ingredient (including any ester or salt of the active ingredient)" refers to the active moiety of the drug for which the applicable period of exclusivity is in question. *Id.* at 8a-9a. The court found that the agency's interpretation of the word "including" as an indication that what followed was an illustrative list of examples of a broader category was "*linguistically* infeasible even though logically possible." *Id.* at 9a.

The court of appeals then rejected petitioner's interpretation as well. Pointing out that it was the agency's prerogative to choose among reasonable constructions of ambiguous statutory language, the court of appeals explained that it could not accept petitioner's interpretation, even if reasonable, if the court perceived—as it did—"still other reasonable constructions." Pet. App. 9a. The court went on to find, however, that petitioner's construction was not reasonable. The court observed that under petitioner's construction the availability of the maximum period of market protection for a drug would depend on whether FDA had first approved the non-salt, non-ester form of the drug or had instead first approved its salt or ester; under petitioner's construction, "if a pharmaceutical manufacturer developed two usable drugs, one a salt of the other, he could gain extra protection by applying for approval of the acid first, followed by the salt, but not under the reverse sequence." *Id.* at 10a-11a. That reading would "promote[] neither the interests of the research-oriented pharmaceutical industry nor the general drug industry in a rational way, producing instead a windfall depending on an accident of chemical nomenclature." *Id.* at 10a. In short, the court concluded, petitioner's interpretation of the statutory language was "possible linguistically but fails to serve any conceivable purpose"; petitioner could advance "no hypothetical reason why Congress (or indeed any of the interest groups) would have wanted the degree of protection a drug received to turn on this variable sequence." *Ibid.* Accordingly, the court remanded the case to the district court with instructions to remand to the agency for a new interpretation of the statute. *Id.* at 11a.

ARGUMENT

The court of appeals' decision is essentially interlocutory in nature. Review by this Court at this stage would accordingly be premature. Moreover, petitioner's central argument that the statutory language in question here has only a single possible plain meaning is belied by the multiplicity of interpretations supplied by the various parties and courts that have attempted to apply it. The court of appeals' decision to remand this matter to the Food and Drug Administration for a new construction of these complex and ambiguous provisions does not warrant this Court's review.

1. The court of appeals here has not authoritatively interpreted the phrase "active ingredient (including any ester or salt of the active ingredient)" as it occurs in the exclusivity provisions at issue, 21 U.S.C. 355(j)(4)(D)(i) and (v). Although the court rejected the two interpretations put forward by FDA and petitioner respectively, the court did not announce its own interpretation of the statute. It simply suggested that a third construction was possible and left FDA free on remand to choose that reading of the statute or some other reading that the agency might develop upon further consideration.

2. Although petitioner correctly points out that the court of appeals' decision differs from the decision reached by the Federal Circuit in *Glaxo Operations UK Ltd.* v. *Quigg*, 894 F.2d 392 (1990), there is no conflict between the two decisions warranting further review by this Court.

First, and of greatest importance in this case in which petitioner bases its entire argument on what it perceives to be the plain meaning of the particular statutory provisions at issue, the D.C. Circuit here

and the Federal Circuit in *Glaxo* were addressing different statutory provisions that contain somewhat different language.[6] As the court of appeals remarked (Pet. App. 6a), even identical terms in separate sections of the same statute may require different interpretations. Thus, the fact that the Federal Circuit in *Glaxo* interpreted certain statutory language differently from the way the D.C. Circuit here interpreted similar, but not identical, language from a different provision of the same statute does not create a conflict between *Glaxo* and this case.

Second, the provision of Title II of the Hatch-Waxman Amendments at issue in *Glaxo*, 35 U.S.C. 156(f), concerns the eligibility of certain drugs for patent term extensions to compensate for the time taken by the FDA to approve the drug. As such, the interpretation and enforcement of that provision is entrusted to the Commissioner of Patents and Trademarks, and that provision has no bearing on the FDA-administered exclusivity provisions of Title I of the Hatch-Waxman Amendments at issue here. In short, as a

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[6] In *Glaxo* the Federal Circuit construed Title II of the Hatch-Waxman Amendments, which authorizes the Commissioner of Patents and Trademarks to extend the term of a patent on a drug product meeting certain other conditions if the product is the first permitted marketing or use of "the active ingredient * * * of * * * a new drug * * * including any salt or ester of the active ingredient." 35 U.S.C. 156(a)(5)(A) and 156(f)(2). By contrast, the provisions of Title I of the Hatch-Waxman Amendments at issue here provide for two-year exclusivity if an application includes "an active agreement (including any ester or salt of the active ingredient) that has been approved in another application," 21 U.S.C. 355(j)(4)(D)(v), or ten-year exclusivity if an application includes "no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application." 21 U.S.C. 355(j)(4)(D)(i).

result of the holdings in *Glaxo* and this case, the same issue will not be decided differently depending on whether it is litigated in the District of Columbia or Federal Circuit.[7] Accordingly, there is no conflict in the circuits.

3. Petitioner insists that the language of the ten-year exclusivity provision (21 U.S.C. 355(j)(4)(D)(i)) has a single possible plain meaning. Indeed, petitioner asserts that this provision is one that "Petitioner, Respondent, agency counsel from the Department of Justice and three federal courts" have unanimously agreed "could not be clearer." Pet. 3. Petitioner neglects to point out, however, that those parties and courts arrived at at least three entirely different interpretations of two distinct statutory provisions.[8] That diversity of interpretation alone belies petitioner's claim of statutory clarity and explicit congressional intent concerning the scope of the ten-year exclusivity provision, and it confirms the propriety of the court of appeals' decision to remand

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[7] As petitioner notes, " '[m]arket exclusivity' * * * is different from a patent right: While a patent owner can exclude all others from competing with like products, market exclusivity only delays approval of ANDAs or 'paper' NDAs. A second company that obtains NDA approval for an existing product is free to compete even during the 'exclusivity' period." Pet. 6 n.2.

[8] Obviously, petitioner and FDA had conflicting interpretations of the statutory language at issue in this case. The district court provided a third reading. Pet. App. 54a-59a. The two other courts to which petitioner presumably refers are the district court and the court of appeals in *Glaxo Operations UK Ltd.* v. *Quigg*, 706 F. Supp. 1224 (E.D. Va. 1989), aff'd, 894 F.2d 392 (Fed. Cir. 1990), which were interpreting somewhat different language in a different provision of the Hatch-Waxman Amendments. See p. 9, *supra*.

this matter to the agency for a new administrative determination.

Petitioner attacks the court of appeals' conclusion that the language of the exclusivity provisions permits an interpretation other than petitioner's own on the ground that the court mistakenly focused on the two-year provision (21 U.S.C. 355(j)(4)(D)(v)), and "not on the ten-year exclusivity provision applicable to DEPAKOTE." Pet. 18. This bootstrap argument presents petitioner's own desired conclusion —that the ten-year provision applies to its product— as a fact that undermines the court of appeals' holding that the statute is ambiguous. Moreover, as petitioner itself argued below, the exclusivity provisions form a coherent structure in which "every drug falls into one—and only one—of five categories that are defined to be mutually exclusive." Pet. C.A. Br. 26. Thus, the scope of the two-year exclusivity provision (21 U.S.C. 355(j)(4)(D)(v)) is directly relevant to the issue of Depakote's eligibility for the maximum ten-year period of market protection under another provision in the five-part scheme.

Finally, petitioner insists that the court of appeals' decision fails to accord the market exclusivity provisions "the presumption of validity to which they are entitled." Pet. 21. Certainly no one, least of all the court of appeals, has suggested that the exclusivity provisions are invalid. Petitioner's argument is really only a reprise of its central contention that the ten-year exclusivity provision has a single possible plain meaning that the court of appeals failed to apply. Once the court identified an ambiguity in the statutory language, it reached the unexceptionable conclusion that it must permit the agency to make the choice among reasonable alternative constructions. Pet. App. 9a.

The court's additional finding that petitioner's interpretation was unreasonable in light of its practical consequences, although not necessary to the court's decision to remand this matter to the agency, was correct. As the court noted, petitioner has failed to advance "*any* scientific, technical, economic or other explanation why Congress would intend the grant of a ten year market exclusivity to depend on the temporal sequence in which * * * applications were approved." Pet. App. 10a. Moreover, every adjudicative body to consider the question—the FDA, the district court, and the court of appeals—has concluded that interpretations of the statutory language other than that of petitioner are possible. Unlike petitioner's proposed interpretation, none of those other interpretations makes market exclusivity turn on entirely arbitrary factors involving the order in which various chemical forms of a drug are approved. The court of appeals thus correctly concluded that petitioner's interpretation is unreasonable.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

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* The Solicitor General is disqualified in this case.

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